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09/262,126	03/03/1999	BRIAN S. MILLER	GC396-2	8961

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EXAMINER	
RAO, MANJUNATH N	
ART UNIT	PAPER NUMBER
1652	20

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/262,126	Applicant(s) MILLER ET AL.	
	Examiner Manjunath N Rao	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-15 and 27-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 5-8, 11, 13-15, 27-30, 33-40* is/are rejected.

7)☒ Claim(s) *9,10,12,31 and 32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1, 3, 5-15 and 27-40 are still at issue and are present for examination.

Applicants' arguments filed on 12-4-01, paper No. 18, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-15, 27-40 in Paper No. 18 is acknowledged. The traversal is on the ground(s) that coexamination of all of Groups I-III would not be serious burden to the Examiner. This is not found persuasive because while the searches for the three groups may overlap, they are not coextensive. The search for Groups II and III would each require the search of subclasses unnecessary for the search of elected Group II. For example, search of Group II would require search of subclass 435/320.1 and search of Group III would require search of subclass 435/275. Furthermore the searches also involve extensive non-patent literature.

The requirement is still deemed proper and is therefore made FINAL.

The traversal is also rendered moot as applicants have cancelled all non-elected claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-8 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 6-8 and 11 recites the limitation "modification" in line 1. There is insufficient antecedent basis for this limitation in the claim due to the amendment to claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 27, 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Ara et al. (Biosci. Biotech. Biochem., Vol. 60(4):634-639, 1996). This rejection is based upon the public availability of a printed publication. Claims 1, 27, 38 are drawn to a truncated pullulanase isolated from a bacillus sp. selected from the group consisting of *B. subtilis*, *B.deramificans*, etc. in which up to 300 amino acids from the N-terminal are deleted resulting in the truncated pullulanase and an enzymatic composition comprising the same. Ara et al. disclose a truncated pullulanase isolated from a *Bacillus* sp. The amino acid sequence that was deleted results in a 114 Kda protein which would encompass up to 300 amino acids. The reference also discloses composition comprising such truncated enzyme. Thus Ara et al. anticipate claims 1, 27, 38 of this application as written.

Ara does not disclose species.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 3, 5, 11, 13-15, 27, 33-39 are rejected under 35 U.S.C. 102(e) as being anticipated by Deweer et al. (US 6,074,854, filed 12-23-1997, issued on 6-13-2000). This rejection is based upon the public availability of a patent publication. Claims 1-3, 5, 11, 13-15, 27, 33- 39 of the instant application are drawn to a modified pullulanase isolated from either a Gram Positive or Gram negative bacteria which includes *B.deramificans strain* T89.117D, wherein the modified pullulanase has at least one amino acid added to the amino terminus (claim 11), is produced by a host cell comprising the nucleic acid that has 70% identity to SEQ ID NO:1, encoding the mature pullulanase (claims 13-15), a composition comprising the said modified pullulanase (claim 27) further comprising another enzyme such as a glucoamylase isolated from any *Aspergillus* strains such as *A.niger, A.awamori* and *A.foetidus* (claims 33-36), a composition which is in solid form or liquid form or comprising 60% modified pullulanase (claims 37-39). Deweer et al. disclose an identical truncated pullulanase in which the first 29 amino acids have been deleted, or modified by addition of an amino acid to the N-terminal region, isolated from *B.deramificans* T89.117D, produced by a host cell comprising the nucleic acid that has 70% identity to SEQ ID NO:1 encoding the mature pullulanase, a composition comprising the said modified pullulanase further comprising another enzyme such as a glucoamylase isolated from any *Aspergillus* strains such as *A.niger, A.awamori* and *A.foetidus*, a composition which is in solid form or liquid form or comprising 60% modified pullulanase (see the entire document, especially claims 1-21). Thus Deweer et al. anticipate claims 1, 3, 5, 11, 13-14, 27, 33-39 of this application as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 5-8, 11, 13, 14-30, 33-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deweer et al. (US 6, 074, 854 filed 12-23-97, issued 6-13-2000) and McPherson et al. (Biochemical Soc. Trans., 1988, vol. 16(5) :723-724) or Albertson (Biochim. Biophys. Acta, Vol. 1354:35-39, 1997).

This rejection is based on printed publications and a patent. Claims 1, 3, 5-8, 11, 13, 14-30, 33-40 in this instant application are drawn to a modified pullulanase from *B.deramificans* T89.117D, wherein the modification is a deletion of about 100, 200 or 300 amino acids from the amino terminus or the addition of at least one amino acid to the amino terminus of the truncated enzyme, wherein the modified pullulanase is produced by culturing a host cell comprising a nucleic acid which is at least 70% identical to SEQ ID NO:1 encoding a truncated pullulanase wherein the host cell is *B.licheniformis* in which certain proteases are inactivated or eliminated. The claims are also drawn to compositions comprising the above modified pullulanase and compositions further comprising additional enzymes such as glucoamylase isolated from *Aspergillus* strains and wherein the modified pullulanase is 60 or 80% of the composition and wherein the composition is in the solid or liquid form.

Deweer et al. teach a modified pullulanase --wherein the first 29 amino acids are removed-- obtained from a Gram positive bacteria such as *B.deramificans* T89.117D produced by a method of culturing a host cell such as *B.licheniformis* in which certain protease genes have been inactivated. The reference also teaches the modification comprising the addition of at least an amino acid to its N-terminus and the host cell comprising a nucleic acid which is more than 70% identical to the SEQ ID NO:1 (see sequence alignment sent in the previous office action). The reference teaches the compositions either in the solid form or liquid form comprising pullulanase wherein it is of the order of 60% of the total enzyme concentration. The reference also teaches compositions comprising additional enzymes such as glucoamylase isolated from *Aspergillus* strains (see claims in the reference). However, the reference does not teach modification of pullulanase by way of deletion of about 100, 200 or 300 N-terminal amino acids.

McPherson et al. teach that pullulanases are significantly large enzymes when compared to other polysaccharide hydrolases and that this large size reduces the efficiency with which it can function by restricting access to internal alpha 1,6 bonds within highly branched substrates.

The reference teaches that proteolytic digestion and computer-based sequence analyses are being used in the art to define a functional "core" pullulanase. The reference provides sources for such computer based homology searches. As an example the reference provides a schematic illustration of the relative position of the 5 conserved "amylase" regions within a selection of hydrolases in comparison to the *K.pneumoniae* pullulanase. The reference teaches that the long N-terminal region lacks any polysaccharide binding or catalyzing sites. McPherson et al. teach the modification of deleting nearly 170 amino acid residues from the amino terminal end which leads to approximately 30% higher activity than that of the native enzyme.

Albertson et al. also teach the modification of a pullulanase (from *C.saccharolyticus*), wherein nearly 381 nucleotides from the 5' region of the cDNA encoding a pullulanase was deleted resulting in a N-terminal truncated pullulanase. The reference also teaches that the deleted amino acid sequence is not essential for either activity or thermostability.

While both McPherson et al. and Albertson et al. do not teach a pullulanase isolated from a Bacillus, it appears that experiments involving truncation of N-terminal amino acids in pullulanase enzymes was well known in the art. These experiments appears to have been performed to determine the nature and the location of secretion signal, activity, catalytic site, transport across membrane and secretion into liquid medium.

It would have been obvious to one skilled in the art at the time the invention was made to combine the teachings of Deweer et al. with that of McPherson et al. or Albertson et al. to make a modified pullulanase in which N-terminal amino acids have been deleted or few amino acids are added to the N-terminal end. This is because Deweer et al. teach a pullulanase isolated from a Bacillus, *B.deramificans*, which is a very large size enzyme with more than 900 amino acids. McPherson et al. teach a method of increasing the efficiency of large size pullulanase by determining and deleting non-essential amino acids in the N-terminal region and Albertson et al. and McPherson et al. teach that deletion of up to at least 100-300 amino acids does not affect the activity of the enzyme negatively but on the other hand increases the efficiency of the enzyme by nearly 30%. It would also be obvious for one skilled in the art to eliminate or inactivate protease genes in the expression hosts, such as Carlsberg protease or endo Glu C protease as Deweer et al. teach such inactivation of proteases such that the heterologous protein is not digested by the endogenous proteases.

Based on the above teachings, one of ordinary skill in the art would be motivated to delete up to 300 amino acids as McPherson et al. compare and show that N-terminal regions of large pullulanase do not have any conserved sequences for either activity or binding to polysaccharide and cleavage of such non-essential sequences results in higher efficiency of the enzyme and Albertson et al. teach a pullulanase in which N-terminal amino acids have been deleted. One would have a reasonable expectation of success since Deweer et al. provide the nucleic acid encoding the pullulanase from *B.deramificans* in a host cell such as *B. licheniformis* in which protease genes have been inactivated and also provide the compositions comprising up to 60% of pullulanase.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Allowable Subject Matter

Claims 9-10, 12, 31, 32 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 6:30 a.m. to 3:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Manjunath N. Rao
2/8/02

Rebecca Prouty

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600